

REMARKS

Claims 1-55 are currently pending. Claims 1-18, 22-26, 30-51, 54, and 55 have been withdrawn from consideration. Therefore claims 19-21, 27-29, 52, and 53 are under consideration.

Claim Amendments

Claims 20 and 21 have been amended to be written in independent form incorporating the text of claim 1. Claim 27 has been amended to be written in independent form incorporating the text of claim 22. These amendments are supported by the specification as filed, particularly as-filed claims 1 and 22. Claims 20, 21, 27-29, 52, and 53 have been amended to remove the phrase “or a modification or derivative thereof.” Claims 19, 20, 21, 28 and 52 have been amended to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said steroid” and claims 27, 29 and 53 have been amended to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said drug.” These amendments are supported by the specification as filed, particularly at page 38, lines 17-26 and Figure 1B. No new matter has been added by way of these amendments.

Claim Objections

The Examiner has objected to claims 20 and 21 because they depend on withdrawn claim 1. Claims 20 and 21 have been amended to be written in independent form incorporating the text of claim 1.

The Examiner has objected to claim 27 because it depends on withdrawn claim 22. Claim 27 has been amended to be written in independent form incorporating the text of claim 22.

Rejection of claims 20, 21, 27-29, 52, and 53 under 35 U.S.C. § 112, second paragraph

Claims 20, 21, 27-29, 52, and 53 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner is of the opinion that

the phrase “a modification or derivative thereof” is unclear because the specification does not provide a standard for determining the scope of the genres of modifications or derivatives.

While not necessarily agreeing with the Examiner’s reasoning, but rather in a good faith effort to expedite prosecution of the present application, Applicants have amended claims 20, 21, and 27-29, 52, 53 to remove the phrase “or a modification or derivative thereof.”

In light of the present amendments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 20, 21, 27-29, 52, and 53 under 35 U.S.C. § 112.

Rejection of claims 20, 21, and 27 under 35 U.S.C. § 102(b)

The Examiner has rejected claims 20, 21, and 27 under 35 U.S.C. § 102(b) as being anticipated by Harris et al. (1997, US Pat No 5,650,096; “Harris”). Specifically, the Examiner contends that claims 20, 21, and 27 are rejected based on Harris’ teachings of compositions comprising spermidine cholesterol carbamate and one or more colipids because in such a situation, cholesterol can be considered a conjugating agent that is first reacted with cholesterol to form cholesteryl chloroformate; cholesteryl chloroformate is then subsequently reacted with Di-CBz-spermidine to form Di-CBz-spermidine cholesteryl carbamate.

While not necessarily agreeing with the Examiner’s reasoning, but rather in a good faith effort to expedite prosecution of the present application, Applicants have amended claims 20 and 21 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said steroid” and claim 27 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said drug.” The present amendments are supported by the specification as filed, particularly at page 38, lines 17-26 and Figure 1B.

Applicants respectfully submit that Harris does not anticipate presently amended claims 20, 21 and 27 of invention for the following reasons. “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” MPEP §2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). “The identical invention must be shown in as complete detail as is contained in the . . . claim.” *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989) (emphasis added)). Therefore, Harris must describe each and every element of the rejected claims in order to anticipate this claim under 35 U.S.C. §102(b). This

reference does not satisfy this requirement. Claims 20, 21, and 27 are product-by-process claims, and as such, are not limited to the manipulations of the recited steps, but only the structure implied by the recited steps. See MPEP § 2113. Applicants respectfully submit that Harris does not anticipate presently amended claims 20, 21 and 27 of invention for the following reasons.

The disclosure of Harris is not an enabling disclosure. Although Harris describes a genus with a vast number of potential members, Harris does not demonstrate the attachment of a polyamine through the C-21 position of a steroid. Only if a species can be “at once envisaged” from a generic chemical formula, can the generic chemical formula serve to anticipate the species. See MPEP 2131.02. When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, *e.g.*, select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990); see also MPEP 2131.02. If one of ordinary skill in the art is able to “at once envisage” the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be “at once envisaged.” See MPEP 2131.02.

Harris describes attachment of a variety of constituents to the C-3 position (Harris, Figures 1, 2, 3, 4, 5, 6, 13, 14) and the C-24 position (Harris, Figure 22) of a steroid. Harris does not demonstrate the attachment of a polyamine through the C-21 position of a steroid.

Because Harris describes a genus with a vast number of potential members, but does not demonstrate the attachment of a polyamine through the C-21 position of a steroid, Harris does not disclose each and every element of Applicants' presently claimed invention and, therefore, does not anticipate the claimed invention. In light of the present amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 20, 21, and 27 under 35 U.S.C. § 102(b).

Rejection of claims 20, 21, and 27 under 35 U.S.C. § 102(e)

The Examiner has rejected claims 20, 21, and 27 under 35 U.S.C. § 102(e) as being anticipated by Mahato et al. (2004, US Pat No 6,696,038; “Mahato”). Specifically, the Examiner contends that Mahato teaches a cationic lipopolymer made by reacting cholesteryl chloroformate with a cationic polyamine because in such a situation, chloroform can be considered a conjugating agent that is first reacted with cholesterol to form cholesteryl chloroformate; cholesteryl chloroformate is then subsequently reacted with the polyamine to form the final product.

While not necessarily agreeing with the Examiner’s reasoning, but rather in a good faith effort to expedite prosecution of the present claims, Applicants have amended claims 20 and 21 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said steroid” and claim 27 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said drug.” The present amendments are supported by the specification as filed, particularly at page 38, lines 17-26 and Figure 1B.

Applicants respectfully submit that Mahato does not anticipate presently amended claims 20, 21 and 27. “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” MPEP §2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). “The identical invention must be shown in as complete detail as is contained in the . . . claim.” *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989) (emphasis added)). Therefore, Mahato must describe each and every element of the rejected claims in order to anticipate this claim under 35 U.S.C. §102(e). This reference does not satisfy this requirement. Applicants respectfully submit that Mahato does not anticipate presently amended claims 20, 21 and 27 of invention for the following reasons.

Mahato does not disclose attachment of a polyamine through the C-21 position of a steroid. Because Mahato does not disclose attachment of a polyamine through the C-21 position of a steroid, it does not disclose each and every element of Applicants' presently claimed invention and, therefore, does not anticipate the claimed invention.

In light of the present amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 20, 21, and 27 under 35 U.S.C. § 102(e).

Rejection of claims 20, 21, and 27 under 35 U.S.C. §103(a)

The Examiner has rejected claims 20, 21, and 27 under 35 U.S.C. §103(a) as being obvious over Wolff et al. (1999, US Pat No 5,965,434; “Wolff”). The Examiner states that Wolff teaches amphipathic lipid compounds comprising a cationic, pH-sensitive, hydrophilic moiety; the lipid portion can be a sterol or steroid (*e.g.*, dexamethasone); the cationic portion comprises a primary, secondary, or tertiary amine; the cationic portion is joined to the lipid by a linker. The Examiner concedes that Wolff does not explicitly disclose the combination of either of the dexamethasone derivatives with a colipid, but argues that Wolff envisions the formation of vesicles comprising a colipid such as phosphatidyl ethanolamine or dioleoylphosphatidyl ethanolamine (*i.e.*, DOPE). Therefore, the Examiner contends that it would have been obvious to one of skill in the art to use the teachings of Wolff to arrive at the present invention.

While not necessarily agreeing with the Examiner’s reasoning, but rather in a good faith effort to expedite prosecution of the present application, Applicants have amended claims 20 and 21 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said steroid” and claim 27 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said drug.” The present amendments are supported by the specification as filed, particularly at page 38, lines 17-26 and Figure 1B.

Applicants respectfully submit that Wolff does not render Applicants’ presently amended claims 20, 21 and 27 unpatentable. The test which must be met for a reference or a combination of references to establish obviousness has not been satisfied in the instant matter. The MPEP states, in relevant part, the proper test for obviousness:

Office policy is to follow *Graham v. John Deere Co.* in the consideration and determination of obviousness under 35 U.S.C. 103... [T]he four factual inquiries enunciated therein as a background for determining obviousness are as follows:

- (A) Determining the scope and contents of the prior art;
- (B) Ascertaining the differences between the prior art and the claims in issue;
- (C) Resolving the level of ordinary skill in the pertinent art; and
- (D) Evaluating evidence of secondary considerations. MPEP § 2141.

Additionally, MPEP § 2143.01 provides: "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). (emphasis added). None of these criteria have been met here.

In *KSR Int'l Co.*, the US Supreme Court restated the requirements for a finding of obviousness. Encouraging the application of common knowledge and common sense, the Court took care to guard against hindsight bias and *ex post* reasoning and to distinguish the predictable from the unpredictable arts ("If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability." [Emphasis added]). The field of cationic nonviral delivery vehicles can only be viewed as a highly unpredictable art (in contrast to the throttle pedals of KSR). Because the skilled person in this art understands the significant unpredictability associated with cationic nonviral delivery vehicles and their methods of use, the rejection of the claims under §103 could only have been made with hindsight bias and *ex post* reasoning in the face of the Applicants' success.

Moreover, when applying 35 U.S.C. § 103, the following tenets of patent law must be followed: 1) the claimed invention must be considered as a whole; 2) the references must be considered as a whole; 3) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and 4) reasonable expectation of success is the standard with which obviousness is determined. MPEP § 2141 II.

Wolff does not expressly teach or suggest all of the claim limitations of the presently-amended claims of the instant application. To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2141.

Wolff discloses the attachment of a primary, secondary, or tertiary amine to a steroid, but Wolff does not disclose or contemplate the attachment of a polyamine through the C-21 position of a steroid.

In light of the present amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 20, 21, and 27 under 35 U.S.C. § 103(a).

Rejection of claim 19 under 35 U.S.C. §103(a)

The Examiner has rejected claim 19 under 35 U.S.C. §103(a) as being obvious over Wolff et al. (1999, US Pat No 5,965,434; “Wolff”) in view of Chaudhary et al., (1997, US Pat No 5,614,503; “Chaudhary”). The Examiner concedes that Wolff does not teach a lipid comprising dexamethasone conjugated to spermidine. However, it is the Examiner’s view that Chaudhary teaches a cationic lipid comprising a lipid tail (such as a steroid) conjugated to a polyamine (such as spermine). The Examiner concedes that Chaudhary does not teach dexamethasone as a lipid moiety, but contends that there would have been a reasonable expectation of success in making a dexamethasone-spermine composition based on the teachings of Wolff and Chaudhary.

While not necessarily agreeing with the Examiner’s reasoning, but rather in a good faith effort to expedite prosecution of the present application, Applicants have amended claim 19 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said steroid.” The present amendments are supported by the specification as filed, particularly at page 38, lines 17-26 and Figure 1B.

Applicants respectfully submit that Wolff, in light of Chaudhary, does not render Applicants’ presently amended claim 19 unpatentable. The test which must be met for a reference or a combination of references to establish obviousness is shown above and not repeated here. The test has not been satisfied in the instant matter.

Neither Wolff nor Chaudhary, alone or in combination, disclose all of the claim limitations of the presently-amended claims of the instant application. To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2141.

Wolff discloses the attachment of a primary, secondary, or tertiary amine to a steroid, but Wolff does not disclose or contemplate the attachment of a polyamine to C-21 of a steroid. Chaudhary discloses the attachment of a spermine to a lipid, but Chaudhary does not disclose the attachment of a polyamine through the C-21 position of a steroid.

In light of the present amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 19 under 35 U.S.C. § 103(a).

Rejection of claim claims 27, 28, 29, 52, and 53 under 35 U.S.C. §103(a)

The Examiner has rejected claims 27, 28, 29, 52, and 53 under 35 U.S.C. §103(a) as being obvious over Harris et al., or Mahato et al., or Wolff et al., when any one of these references is combined with Lin et al. (2003, U.S. 6,517,828; “Lin”). The Examiner is citing Lin for the purpose of demonstrating that Lin teaches a kit and therefore it would have been obvious of a skilled artisan to organize the elements set forth in any of Harris et al., or Mahato et al., or Wolff et al., into a kit.

While not necessarily agreeing with the Examiner’s reasoning, but rather in a good faith effort to expedite prosecution of the present application, Applicants have amended claims 28 and 52 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said steroid” and claims 27, 29, and 53 to recite “wherein said conjugating reagent conjugates said polyamine through the C-21 position of said drug.” The present amendments are supported by the specification as filed, particularly at page 38, lines 17-26 and Figure 1B.

Applicants respectfully submit that neither Harris, nor Mahato, nor Wolff, combined with Lin, renders Applicants’ presently amended claims 27, 28, 29, 52, and 53 unpatentable. The test which must be met for a reference or a combination of references to establish obviousness is shown above and not repeated here. The test has not been satisfied in the instant matter.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2141.

As discussed above, none of the primary references (*i.e.*, Harris, Mahato, Wolff) disclose all of the claim limitation of the presently-amended claims of the instant application. Specifically, none of the primary references (*i.e.*, Harris, Mahato, Wolff) disclose the attachment of a polyamine through the C-21 position of a steroid. Lin also does not disclose attachment of a polyamine through the C-21 position of a steroid. Thus, Lin, does not correct the deficiencies of the primary references.

In light of the present amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 27, 28, 29, 52, and 53 under 35 U.S.C. § 103(a).

Summary

Applicants respectfully submit that the amendments made to the claims and the specification herein do not introduce new matter, and that the arguments set forth herein evidence that the pending claims are in full condition for allowance. Accordingly, favorable examination of the claims is respectfully requested at the earliest possible time.

Respectfully submitted,
SCOTT L. DIAMOND, *et al.*

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KATHRYN DOYLE, Ph.D., J.D.
Registration No. 36,317
DRINKER, BIDDLE & REATH, LLP
One Logan Square
18th and Cherry Streets
Philadelphia, PA 19103-6996
Telephone: (215) 988-2700
Direct Dial: (215) 988-2902
Facsimile: (215) 988-2757
E-Mail: Kathryn.Doyle@dbr.com
Attorney for Applicants